REMARKS

Applicant respectfully requests reconsideration. Claims 1, 2, 5-7, 9, 11-17, 19-34, 68, 91 and 125-130 were previously pending in this application. Claims 1, 91, 125, 126 and 129 have been amended. Support for the amendment can be found at least in Fig.1, page 7, lines 10-12 and in claims 8 and 127 as originally filed. Claim 127 has been canceled. No new claims have been added. As a result, claims 1, 2, 5-7, 9, 11-17, 19-34, 68, 91, 125, 126 and 128-130 are pending for examination with claims 1, 68, 91, 125, 126, 129 and 130 being independent claims. No new matter has been added. Applicant reserves the right to pursue the subject matter of the claims prior to the amendments in one or more continuing applications.

Rejections Under 35 U.S.C. §102

Claims 1, 2, 5-7, 11, 14, 16, 24-26, 31, 91 and 126-129 are rejected under 35 U.S.C. §102(b) as being anticipated by Cheng et al. (Biochemical and Biophysical Research Communications, 1991, 174(2):785-789). According to the Examiner, Cheng et al. teaches a method for analyzing a nucleic acid polymer, including all the limitations of claims 1, 2, 5-7, 11, 14, 16, 24-26, 31, 91 and 126-129.

Applicant respectfully traverses. Cheng et al. does not teach all the steps of the rejected claims and therefore Cheng et al. does not anticipate the rejected claims. However, without conceding to the Examiner's position and merely in the interest of expediting prosecution, Applicant has amended independent claims 1, 91, 126 and 129 to include the step "providing a conjugate comprising a nucleic acid tag molecule and a nucleic acid binding enzyme". Support for the amendment can be found in the specification at least in Fig. 1 and page 7, lines 10-12.

The teachings of Cheng et al. relate to the binding of a reverse transcriptase to an RNA/DNA substrate, and the subsequent cross-linking of the reverse transcriptase to the RNA/DNA substrate. As a first step the substrate is generated by binding of the DNA primer (the "nucleic acid tag molecule", according to the Examiner) to the RNA template (the "nucleic acid polymer", according to the Examiner). The next step includes the binding of the reverse transcriptase followed by its cross-linking to the RNA/DNA substrate, resulting in the formation of a conjugate. Cheng et al. does not teach the step of "providing a conjugate comprising a nucleic acid tag molecule and a

nucleic acid binding enzyme", as the conjugate of Cheng et al. is only generated after binding and cross-linking to the RNA/DNA substrate, *i.e.*, after the contacting step has been performed. Since Cheng et al. does not teach all the steps of the rejected claims, Cheng et al. does not anticipate these claims.

Accordingly, reconsideration and withdrawal of this rejection is respectfully requested.

Claim 125 is rejected under 35 U.S.C. §102(b) as being anticipated by U.S. Patent No. 6,362,328 to Fisher et al. as evidenced by Chaudhry et al. (Nucleic Acids Research (1995) 23(19): 3805-3809). According to the Examiner, Fisher et al. teaches a method of analyzing a nucleic acid polymer comprising using a conjugate consisting of a covalently linked oligonucleotide and a nuclease. Further, according to the Examiner, Chaudhry et al. teaches that a nuclease is a repair enzyme.

Applicant respectfully traverses. Fisher et al. does not teach all the steps of the rejected claim, and therefore Fisher et al. does not anticipate this claim. The rejected claim comprises the step of "allowing the nucleic acid binding agent to bind to the nucleic acid polymer non-specifically", which is not taught by Fisher et al.

Fisher et al. teaches a conjugate of "a single binding member" coupled to a nuclease (column 2, lines 55-61). In preferred embodiments the single binding member is an antibody or a nucleic acid. Fisher et al. does not teach that the nuclease binds the larger nucleic acid. Quite to the contrary, Fisher et al. refer to the nucleic acid probe as a "single binding member", thereby stating that the conjugate comprises only *one* binding member and that binding member is not the nuclease. Fisher et al. clearly and repeatedly states that the nuclease within the conjugate functions as a label. Upon binding of a single binding member that is the nucleic acid probe to a target nucleic acid polymer, the nuclease catalyzes the phosphorylation of a substrate resulting in a detectable signal. There is no teaching in Fisher et al. that the nuclease binds to the target nucleic acid polymer.

Thus, Fisher et al. does not teach the step "allowing the nucleic acid binding agent to bind to the nucleic acid polymer non-specifically". Since Fisher et al. does not teach all the steps of the rejected claim, Fisher et al. does not anticipate this claim.

Accordingly, reconsideration and withdrawal of this rejection is respectfully requested.

Rejections Under 35 U.S.C. §103

Claims 1, 2, 5-7, 9, 11-15, 21-28, 30, 31, 91 and 126-130 are rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 6,362,328 to Fisher et al. as evidenced by Chaudhry et al. (*Nucleic Acids Research* (1995) 23(19): 3805-3809) in view of U.S. Patent No. 5,965,361 to Kigawa et al. According to the Examiner, Fisher et al. teaches a method for analyzing a nucleic acid polymer comprising all the limitations of the rejected claims, except for a method that does not depend on the catalytic activity of the nuclease and a method for labeling the nucleic acid tag molecules and nucleic acid binding enzymes with detectable moieties. However, according to the Examiner, Kigawa et al. teaches methods of analyzing a nucleic acid polymer that do not rely on the catalytic activity of the nucleic acid binding enzyme and labeling with detectable moieties. Also, according to the Examiner, it would have been obvious to apply the teachings of Kigawa et al. to Fisher et al. because combining the teachings would result in a faster and simpler method for labeling a nucleic acid polymer. Finally, according to the Examiner, an ordinary artisan would have a reasonable expectation of success because the methods of Kigawa et al. and Fisher et al. are directed to the same problem.

Applicant respectfully traverses. The Examiner has not met her burden in establishing a *prima facie* obviousness rejection. While the Examiner discusses why it would have been obvious to apply the teachings of Kigawa et al. pertaining to labeling with detectable moieties, to Fisher et al., the Examiner does not discuss why it would be obvious to apply the teachings of Kigawa et al. pertaining to methods of analyzing a nucleic acid polymer *that do not rely on the catalytic activity of the nucleic acid binding enzyme*, to the teachings of Fisher et al.

Furthermore, even if such reasoning existed (and Applicant contends that none does), the combination of Kigawa et al. and Fisher et al. does not yield each and every limitation of the rejected claims because the combination does not teach a conjugate comprising a nucleic acid tag molecule and a nucleic acid binding agent wherein *the nucleic acid binding agent binds to a nucleic acid polymer non-specifically*.

The Examiner points to column 4, lines 37-53 of Fisher et al. to support the argument that Fisher et al. discloses "allowing the nucleic acid binding enzyme to bind to the nucleic acid polymer

non-specifically and translocate along the polymer". However, these paragraphs pertain to methods of nucleic acid synthesis and the binding of the nucleic acid tag molecule to a nucleic acid polymer. They do not disclose non-specific binding of a nucleic acid binding enzyme to a nucleic acid polymer. Furthermore, while Fisher et al. discloses a conjugate comprising a nucleic acid tag molecule and a nuclease ("nucleic acid binding enzyme"), the nuclease does not function as a nucleic acid binding agent but rather functions as a label. Thus, the "nucleic acid binding enzyme" of Fisher et al. does not bind to a nucleic acid polymer non-specifically.

The Examiner points to column 2, lines 39-44 and column 17, lines 5-25 of Kigawa et al. to support the argument that Kigawa et al. discloses "allowing the nucleic acid binding enzyme to bind to the nucleic acid polymer non-specifically and translocate along the polymer". However, these paragraphs pertain to methods of binding of the nucleic acid tag molecule to a nucleic acid polymer. They do not disclose non-specific binding of a nucleic acid binding enzyme to a nucleic acid polymer, at least because RecA only binds to the location bound by the probe.

Thus, the combination does not disclose a nucleic acid binding enzyme that can bind to a nucleic acid non-specifically, and it therefore cannot disclose a conjugate comprising a nucleic acid tag molecule and a nucleic acid binding agent wherein *the nucleic acid binding agent binds to a nucleic acid polymer non-specifically*.

Finally, a person of ordinary skill in the art would have no expectation of success when combining the teachings of Fisher et al. and Kigawa et al. Fisher et al. teaches the use of an enzyme as a label, while Kigawa et al. teaches the use of an enzyme as an agent to bind a probe to a target nucleic acid. Thus, a person of ordinary skill in the art would not expect that replacing an enzyme used as label, by an enzyme used as agent to bind a probe to a target nucleic acid would be successful.

For at least these reasons, the combination of Fisher et al. and Kigawa et al. does not render obvious the rejected claims.

Accordingly, reconsideration and withdrawal of this rejection is respectfully requested.

Claims 1, 2, 5-7, 9, 11-13, 16, 17, 22-31, 91 and 126-130 are rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 6,362,328 to Fisher et al. as evidenced by

Chaudhry et al. (*Nucleic Acids Research* (1995) 23(19): 3805-3809) in view of Rye et al. (*Nucleic Acids Research* (1992) 20(11): 2803-2812) and further in view of U.S. Patent No. 6,348,317 to Thompson et al.

According to the Examiner, Fisher et al. teaches a method for analyzing a nucleic acid polymer comprising all the limitations of the rejected claims, except for labeling the nucleic acid polymer with a backbone specific label and labeling the nucleic acid tag molecule with a fluorophore agent or photocleaving agent. However, according to the Examiner, Rye et al. teaches fluorescent intercalators, which are backbone specific labels and photocleaving agents, as evidenced by Thompson et al.

Applicant respectfully traverses. The combination of Fisher et al., Rye et al. and Thompson et al. does not render obvious the rejected claims at least because the combination of Fisher et al., Rye et al. and Thompson et al. does not teach all the elements of the rejected claims. At a minimum, the combination does not teach a conjugate comprising a nucleic acid tag molecule and a nucleic acid binding agent wherein *the nucleic acid binding agent binds to a nucleic acid polymer non-specifically*.

As stated above, Fisher et al. does not teach a conjugate comprising a nucleic acid tag molecule and a nucleic acid binding agent where the nucleic acid binding agent binds to a nucleic acid polymer non-specifically. The teachings of Rye et al. and Thompson et al. do not supply the missing teachings because these references merely relate to fluorescent dyes. For at least this reason, the combination of Fisher et al., Rye et al. and Thompson et al. does not render obvious the rejected claims.

Accordingly, reconsideration and withdrawal of this rejection is respectfully requested.

Claims 19, 20, 33, and 34 are rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 6,362,328 to Fisher et al. as evidenced by Chaudhry et al. (*Nucleic Acids Research* (1995) 23(19): 3805-3809) in view of U.S. Patent No. 5,965,361 to Kigawa et al. and further in view of PCT Publication No. WO 00/09757 to Tegenfeldt et al.

According to the Examiner, the combination of Fisher et al., Chaudhry et al. and Kigawa et al. teaches all the limitations of the rejected claims, except for a linear polymer analysis system for

optically analyzing polymers. However, according to the Examiner, Tegenfeldt et al. teaches a linear polymer analysis system.

Applicant respectfully traverses. The combination of Fisher et al., Chaudhry et al., Kigawa et al. and Tegenfeldt et al. does not render obvious the rejected claims at least because the combination of Fisher et al., Chaudhry et al., Kigawa et al. and Tegenfeldt et al. does not teach all the elements of the rejected claims. At a minimum, the combination does not teach a conjugate comprising a nucleic acid tag molecule and a nucleic acid binding agent wherein *the nucleic acid binding agent binds to a nucleic acid polymer non-specifically*.

As stated above, the combination of Fisher et al., Chaudhry et al., and Kigawa et al. does not teach a conjugate comprising a nucleic acid tag molecule and a nucleic acid binding agent where the nucleic acid binding agent binds to a nucleic acid polymer non-specifically. Tegenfeldt et al. does not supply the missing teaching. For at least this reason, the combination of Fisher et al., Chaudhry et al., Kigawa et al. and Tegenfeldt et al. does not render obvious the rejected claims.

Accordingly, reconsideration and withdrawal of this rejection is respectfully requested.

Claim 32 is rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 6,362,328 to Fisher et al. as evidenced by Chaudhry et al. (*Nucleic Acids Research* (1995) 23(19): 3805-3809) in view of U.S. Patent No. 5,965,361 to Kigawa et al. and further in view of Gite et al. (*Journal of Molecular Recognition* (1995) 8: 281-289).

According to the Examiner, the combination of Fisher et al., Chaudhry et al. and Kigawa et al. teaches all the limitations of the rejected claim, except for detecting the nucleic acid binding enzyme using an antibody. However, according to the Examiner, Gite et al. teaches detecting a nucleic acid binding enzyme using an antibody.

Applicant respectfully traverses. The combination of Fisher et al., Chaudhry et al., Kigawa et al. and Gite et al. does not render obvious the rejected claims because the combination of Fisher et al., Chaudhry et al., Kigawa et al. and Gite et al. does not teach all the elements of the rejected claims. At a minimum, the combination does not teach a conjugate comprising a nucleic acid tag molecule and a nucleic acid binding agent wherein *the nucleic acid binding agent binds to a nucleic acid polymer non-specifically*.

As stated above, the combination of Fisher et al., Chaudhry et al., and Kigawa et al. does not teach a conjugate comprising a nucleic acid tag molecule and a nucleic acid binding agent where the nucleic acid binding agent binds to a nucleic acid polymer non-specifically. The teaching of Gite et al. does not supply the missing teachings because Gite et al. merely relates to detecting a nucleic acid binding enzyme using an antibody. For at least this reason, the combination of Fisher et al., Chaudhry et al., Kigawa et al. and Gite et al. does not render obvious the rejected claim.

Accordingly, reconsideration and withdrawal of this rejection is respectfully requested.

Claim 68 is rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 6,362,328 to Fisher et al. in view of U.S. Patent No. 5,965,361 to Kigawa et al. and further in view of PCT Publication No. WO 00/09757 to Tegenfeldt et al.

According to the Examiner, the combination of Fisher et al., Chaudhry et al. and Kigawa et al. teaches all the limitations of the rejected claim, except for a linear polymer analysis system for optically analyzing polymers. However, according to the Examiner, Tegenfeldt et al. teaches a linear polymer analysis system.

Applicant respectfully traverses. The combination of Fisher et al., Chaudhry et al., Kigawa et al. and Tegenfeldt et al. does not render obvious the rejected claims because the combination of Fisher et al., Chaudhry et al., Kigawa et al. and Tegenfeldt et al. does not teach all the elements of the rejected claims. Ata minimum, the combination does not teach a conjugate comprising a nucleic acid tag molecule and a nucleic acid binding agent wherein *the nucleic acid binding agent binds to a nucleic acid polymer non-specifically.*

As stated above, the combination of Fisher et al., Chaudhry et al., and Kigawa et al. does not teach a conjugate comprising a nucleic acid tag molecule and a nucleic acid binding agent where the nucleic acid binding agent binds to a nucleic acid polymer non-specifically. Tegenfeldt et al. does not supply the missing teachings. For at least this reason, the combination of Fisher et al., Chaudhry et al., Kigawa et al. and Tegenfeldt et al. does not render obvious the rejected claim.

Accordingly, reconsideration and withdrawal of this rejection is respectfully requested.

CONCLUSION

A Notice of Allowance is respectfully requested. The Examiner is requested to call the undersigned at the telephone number listed below if this communication does not place the case in condition for allowance.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, the Director is hereby authorized to charge any deficiency or credit any overpayment in the fees filed, asserted to be filed or which should have been filed herewith to our Deposit Account No. 23/2825, under Docket No. C0989.70054US00.

Dated: May 28, 2008

Respectfully submitted,

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